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THE SCHOOL OF MEDICINE

Department of Pediatrics
1740 Bainbridge Street

November 26, 1946

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Washington University School of Medicine
St. Louis, Mo.

Dear Sol:

I wish to make clear at the beginning that I told Willard nothing about the cytogene. My sole conditioning attempt was on the question of the growth of root beer bottles.

You sent Jesse's letter to me and mine to Jesse. We have now switched. Your stuff sounds exciting if the enzymes prove to be nucleic acid specific. However it's really something to worry about. Kunitz's ribonuclease is crawling with proteolytic activity so that doesn't help. I have no ribonuclease free of proteolytic activity. However a paper appeared in the J.B.C. some months back on soy bean ribonuclease by some people from Michigan. This stuff may be pure in that sense, so write them. Furthermore Margaret Mac Donald at Cold Spring Harbor is trying to free the Kunitz enzyme from proteolytic activity so you might write her.

The simplest test for proteolytic activity would be a reduction of gelatin viscosity. At 0.2% per cc McCarty's DNase in his medium does not reduce the viscosity of gelatin in several hours although very active on DNA. I'm sending some of his enzyme and some polymerized NaDN which appears biuret free and seems pretty good. I have been using this at 0.2% to control DNase solutions. See Kunitz JBC paper this year on the ribonuclease assay.

I am also sending some of Kunitz's pure chymotrypsin and trypsin. The latter contains 40% $MgSO_4$. I don't know if they're ribonuclease free. I have made stock solutions at 0.1% of all the enzymes in H_2O, and stored them in the icebox. Every week we'd make new stocks. DNase especially goes to pot on storage; the others appear stable.

The only case I know of where the two nucleic acids appear together, perhaps, is a nucleoprotein from tubercle bacillus isolated by Chargaff. I think your situation is dubious since ribonuclease has never been observed to degrade RNA in ribonucleoprotein, but only after destruction of the protein by fixatives, heat, etc.

We've confirmed and extended the 5-methyl tryptophane stuff and I'm writing it up now. The first part of that appeared in the Nov. J. Exp. Med. I'm glad you could get the compound. You'll have to work out your concentrations. We work at 5×10^{-4}M. 5×10^{-6}M tryptophane interferes.

I have been studying NA metabolism during infection and during interference. This stuff appears quite basic since I have demonstrated a stimulated DNA synthesis apparently going thru a ribose-5-phosphate turnover in infection while almost everything else stops dead. With irradiated virus that synthesis is blocked. 5-methyl tryptophane also pulls that latter stunt.

And we have found some growth factors for virus synthesis. One stimulates DNA synthesis and the second, indole-3-acetic acid (but not tryptophane) facilitates the conversion of synthesized DNA to virus. I'm sending off a couple of notes soon on this.

We're having trouble getting radioactive P since MIT stopped producing and Oak Ridge hasn't shipped any. Can you or Martin help in any way?

Regards to Helen, Willard, Martin.

Best,

Seymour

Seymour Cohen

SSC:R